Remarks

Claims 1-3, 5-7 and 91 were rejected under 35 USC §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 92-96 were added to avoid multiple dependency issues. No new matter has been added.

Claims 1 and 3 have been clarified. The term "Gly m Bd 30 K" is defined in the claim in the parenthetical which states "(Soybean vacuolar protein P34)" and in the specification on page 7 at lines 11-14. It is stated that "The terms "P34 (soybean vacuolar protein)" and "Gly m BD 30K" and "Gly m 1" [SEQ ID NO:1] are used interchangeably herein. They all refer to the major soybean seed allergen. Major allergens are generally defined as proteins for which 50% or more of the allergic patients studied have specific IgE." Accordingly, it is respectfully submitted that the term is clear.

Claims 1 and 3 now recite that the isolated nucleic acid fragment corresponds substantially to a transcript encoding all or a part of Gly m Bd 30 K polypeptide and said isolated nucleic acid fragment shares at least 45% sequence identity with the nucleotide sequence set forth in SEQ ID NO:1 wherein the expression of said construct is sufficient to lower the Gly m Bd 30 K content. The term "functionally equivalent subfragment" has been deleted. Support for these changes can be found in the specification on page 8 at lines 30 –38 and on page 10 starting at line 33 through line 12 on page 11. Thus, no new matter has been added.

Regarding the term "hypoallergenic soybean plant", attention is kindly invited to the specification at page 7, lines 35-36 which states that the "term "hypoallergenic" means substantially free of any allergens, i.e., an immunological response, such as an allergic reaction, should not be triggered."

Withdrawal of the rejection of the claims under 35 USC §112, second paragraph is respectfully requested in view of the above amendments and discussion.

Claims 1-3, 5-7 and 91 were rejected under 35 USC §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. It is stated on page 4 of the Office Action that "Applicants do not present a description of the domains that are specific to this particular Soybean vacuolar protein P34 nor domains that are important for its proper function. . . ."

Attention is kindly invited to page 14 of the specification at lines 12 – 23 which states that

> P34 possesses most of the conserved characteristics of cysteine proteases including a large precursor domain that is posttranslationally processed. The primary sequence contains aligned and conserved amino acids that are important in the conserved tertiary conformation of the papain superfamily. P34 exhibits some unique features that separate it from other members of the papain superfamily. Among these are replacement of the conserved cysteine in the active site found in all other papain family proteins with a glycine, suggesting that the protein is enzymatically inactive. Cysteine proteases are typically self-processed under acid-reducing conditions resulting in the cleavage of the large precursor domain. However, P34 is processed after an asparagine residue in a single step, most likely by the same enzyme that processes the 11S storage proteins. Sequence comparisons and alignments indicate that although P34 is a member of the papain superfamily, it is also quite dissimilar from the enzymatically active cysteine proteases including those identified in soybean.

Submitted herewith for the Examiner's convenience is another copy of Kalinksi et al., J. Biol. Chem. 265(23): 13843-13848 (1990), which reports on the deduced sequence of a P34 clone which was believed to encode a polypeptide with close similarity to the thiol proteases of the papain family.

Thus, sufficient identifying characteristics are set forth in the specification and Kalinkski et al. to allow one skilled in the art to predictably determine mutants and allelic variants.

Furthermore, the start and stop codons are identified in the specification and in Kalinski et al. Specifically, it is stated in the specification on page 5 starting at line 36 through line 2 on page 6 that the "sequence starts and ends with the NotI sites that were part of the primer sequences used in the construction of the insert (see Example 1). The promoter that directs the synthesis of P34 in pKS73 is from the beta-conglycinin gene, and the 3'-untranslated region is from the phaseolin gene." The complete cDNA sequence and predicted amino acid sequence of P34 are set forth in Figure 3 on page 13845 of Kalinksi et al.

In view of the foregoing, it is respectfully submitted that the written description is satisfied. Accordingly, withdrawal of this ground of rejection is respectfully requested.

Claims 1-3, 5-7 and 91 were rejected under 35 USC §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Attention is kindly invited to Example 1 which refers to the entire insert from Genbank clone J05560. Attached hereto is a copy of the printout from the NCBI database regarding this insert which also references the Kalinski et al. paper

discussed above. It is clear from the foregoing discussion that the translation start and stop codons have been disclosed

Regarding an assay by which one can test the activity of an isolated protein encoded by the isolated nucleic acid fragments as claimed, attention is kindly invited to Example 4 which is entitled "Assay for ***Gly 1 m*** Content of Transformed Embryos." It was stated on page 7 of the specification that the terms "P34 (soybean vacuolar protein)" and "Gly m BD 30K" and "Gly m 1" [SEQ ID NO:1] are used interchangeably herein.

Example 3 shows that mature somatic soybean embryos are a good model for zygotic embryos. This example is entitled "The Phenotype of Transgenic Soybean Somatic Embryos Is Predictive of Seed Phenotypes From Resultant Regenerated Plants." Thus, the data provided in Example 3 addresses the concern raised on page 6 of the Office Action that "Applicants have not generated a Soybean plant transformed with SEQ ID NO:1 that produces a plant with reduced expression of the endogenous P34 protein, that supposedly acts as an allergen."

Information regarding structural information is provided on page 14 of the specification at lines 12-23 and in Kalinski et al. as was discussed above.

Claims 1 and 3 have been amended to recite that the isolated nucleic acid fragment corresponds substantially to a transcript encoding all or a part of Gly m Bd 30 K polypeptide and said isolated nucleic fragment corresponds substantially to the nucleotide sequence set forth in SEQ ID NO:1 wherein the expression of the construct is sufficient to lower the Gly m Bd 30 K content.

The specification does indeed disclose how a plant transformed with any of the above mentioned sequences will suppress the expression of the endogenous allergenic protein. Attention is kindly invited to Example 8 which is entitled "Coordinated Loss of Both ß- and ß'-Subunits of Beta-Conglycinin in Co-suppressed Transgenic Plants".

Based on the information provided in the specification, it is clear that one of skill in the art can reasonably generate transformed plants having the desired phenotype using a specific isolated gene.

WO 99/15682 which published on April 1, 1999 and WO 98/36083 which published on August 20, 1998 describe gene silencing materials and methods. These publications describe, *inter alia*, the silencing of plant genomic gene expression by introducing expression constructs containing plant viral nucleic acid sequences coupled to whole, or partial, gene sequences homologous to the target genes to be silenced.

WO 99/53050, which published on October 21, 1999, describes chimeric constructs encoding RNA molecules directed towards a target nucleic acid which are

comprised of sense and antisense sequences, such that the expressed RNA is capable of forming an intramolecular double-stranded RNA structure. The expression of these RNA in transgenic organisms results in gene silencing of the all homologous target nucleic acid sequences within the cell.

Copies of these publications are enclosed herewith for the Examiner's convenience.

Given the foregoing, it is respectfully submitted that the one skilled in the art can make and use the claimed invention without engaging in undue experimentation. Thus, withdrawal of the rejection of the claims under 35 USC §112, first paragraph, is respectfully requested.

Claims 7 and 91 have been amended to recite that the seeds comprise the construct introduced into the parent seed. These claim amendments are believed to obviate the rejection under 35 USC §101.

Claim 1 was rejected under 35 USC §102 (b) as being anticipated by Kawai et al. (May 13, 1997, Japanese Patent Number JP409121870A). The terms "fragment that substantially corresponds to SEQ ID NO:1" and "functionally equivalent subfragment thereof" have been deleted from claim 1.
The claim now recites that the isolated nucleic acid fragment corresponds substantially to a transcript encoding all or a part of Gly m Bd 30 K polypeptide and said isolated nucleic acid fragment shares at least 45% sequence identity with the nucleotide sequence set forth in SEQ ID NO:1 wherein the polypeptide encoded is sufficient to lower the Gly m Bd 30 K content.

Since Kawai et al. teach a thiol protease encoding a nucleic acid sequence that exhibits 14.4% identity with SEQ ID NO:1 of the instant invention, it does not anticipate the claimed invention which recites that at least 45% sequence identity with the nucleotide sequence set forth in SEQ ID NO:1.

Accordingly withdrawal of the rejection of the claims under 35 USC §102(b) is respectfully requested.

Claims 1-3, 5-7 and 91 were rejected under 35 USC §103(a) as being unpatentable over Kawai et al. as discussed above, and further in view of Kinney et al. WO 97/47731, listed in the IDS.

Kawai is discussed above.

WO 97/47731 concerns suppression of specific classes of soybean protein genes to effect a change in seed storage protein profile of transgenic plants because modification of the seed storage protein profile can result in the production of novel soy protein products with unique characteristics. U.S. Patent No. 6,362,399, issued March 26, 2002, relates to WO 97/47731. The '399 patent claims a soybean plant transformed at a single locus in its genome with a chimeric gene comprising at least

a portion of a glycinin or a beta conglycinin gene wherein said transformation results in reduction of the amount of at least one soybean seed storage protein, selected from the group consisting of glycinin and beta-conglycinin, in seed obtained from said transformed plant when compared to the amount of soybean seed storage protein in seed obtained from a non-transformed plant. Kinney does **not** teach or suggest lowering the P34 content of a soybean.

As was discussed above, Kawai teach a thiol protease encoding a nucleic acid sequence that exhibits 14.4% identity with SEQ ID NO:1 of the instant invention. Kawai does not anticipate or render obvious the claimed invention which recites that at least 45% sequence identity with the nucleotide sequence set forth in SEQ ID NO:1.

It would not have been obvious to one skilled in the art at the time the invention was made to transform a soybean plant with the expression construct of Kawai using any of the heterologous promoters of Kinney to express thiol protease in a soybean plant with a reasonable expectation of success.

The claimed invention concerns a recombinant expression construct to lower Gly m Bd 30K (Soybean vacuolar protein P34) content of a soybean which comprises a promoter operably linked to an isolated nucleic acid fragment corresponding substantially to a transcript encoding all or a part of Gly m Bd 30 K polypeptide and said isolated nucleic fragment shares at least 45% sequence identity with the nucleotide sequence set forth in SEQ ID NO:1 wherein the polypeptide encoded is sufficient to lower the Gly m Bd 30 K content.

Kawai teaches a thiol protease encoding a nucleic acid sequence having about 14.4% identity with the instant SEQ ID NO:1. In contrast, the claimed invention recites at least 45% sequence with identity with SEQ ID NO:1.

Furthermore, the isolated nucleic acid fragment of the claimed invention corresponds substantially to a transcript encoding all or a part of Gly m Bd 30 K polypeptide and said isolated nucleic fragment shares at least 45% sequence identity with the nucleotide sequence set forth in SEQ ID NO:1 wherein the polypeptide encoded is sufficient to lower the Gly m Bd 30 K content.

Kawai's sequence does not meet these criteria and Kinney is concerned with modifying the seed storage protein content.

The Court of Appeals for the Federal Circuit in In re Dow Chemical Co., 5 USPQ2d 1529, 1531 (Fed. Cir. 1988) has stated that the

> consistent criterion for determination of obviousness is whether the prior art would have suggested to one of ordinary skill in the art that this process should be carried out and would have a reasonable likelihood of success viewed in light of the prior art. . . .

> In determining whether such a suggestion can fairly be gleaned from the prior art, the full field of the invention must be considered; for the person of ordinary skill is charged with knowledge of the entire body of technological literature, including that which might lead away from the claimed invention.

Given the foregoing, it is respectfully submitted that the references, either individually or in combination, do not teach or suggest the claimed invention.

Thus, withdrawal of the rejection of the claims under 35 USC §103 is respectfully requested.

It is respectfully submitted that the claims are now in form for allowance which allowance is respectfully requested.

A petition for a one (1) month extension of time accompanies this response along with copies of Kalinski et al, the NCBI database printout for J05560, WO 99/15682, WO 98/36083, and WO 99/53050 accompany this response.

Please charge any fees or credit any overpayment of fees which are required in connection with the filing of this Response and Petition for Extension of Time to Deposit Account No. 04-1928 (E. I. du Pont de Nemours and Company).

Respectfully submitted,

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Dated: July 1, 2003